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► **To cite this version:**

Farad Khoystatee, Luo Zhongyue, Carole-Anne Volette, Thomas Benneteau, Romain Beaubois, et al..  
NEUROMIMETIC STIMULATION APPLIED ON CEREBRAL ORGANOIDs. 10th International  
Symposium on Microchemistry and Microsystems (ISMM 2018), Jun 2018, Busan, South Korea. hal-  
02484019

**HAL Id: hal-02484019**

**<https://hal.science/hal-02484019v1>**

Submitted on 19 Feb 2020

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# NEUROMIMETIC STIMULATION APPLIED ON CEREBRAL ORGANOIDS

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## INTRODUCTION

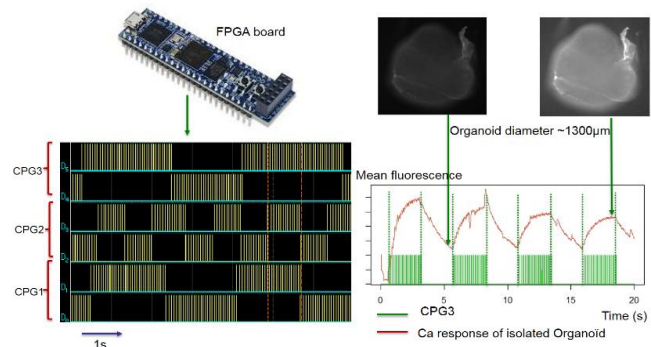
Millions of people are affected by neurological disorders. Brain-Machine Interfaces (BMIs) and neuroprosthesis have been object of extensive research and may represent a valid treatment for diverse neurological diseases. The realization of neuroprostheses requires technologies to interact with neuronal cell assemblies in the nervous system, and to drive them into a desired state or to produce a specific behavior. A hardware set-up that can be used to connect with biological system is a Spiking Neural Network (SNN) system which implements biologically realistic neural network models, spanning from the electrophysiological properties of one single neuron up to network plasticity rules. In this work, we present a digital hardware implementation of a biomimetic SNN reproducing a Central Pattern generator (CPG) [1] for stimulating organoids [2], [3] which are three-dimensional assemblies of neurons developed from human stem cells in vitro. By connecting organoids mimicking our nervous system with electronic SNNs, we intend to develop a model system for a brain-electronics interface.

## METHODS

Most of rhythmic movements are programmed by central pattern-generating networks that comprise neural oscillators. This CPG consists of two neurons, connected to each other via inhibitory synapses including short term plasticity. We implement real-time biomimetic central pattern generators (CPG) into digital hardware (FPGA). This CPG mimics the Leech heartbeat neural network system [3]. This system is composed of Izhikevich neurons, synaptic and plasticity systems. Our implementation needs few resources, consumes low power, and can be easily embedded. Our system has been validated by comparing to biological data. The CPGs provide bursts of spikes with frequency, variability and spike width in the ranges commonly observed in nature, and thus are optimal for biomimetic stimulations. Cerebral organoids were generated as described before [2]. After loaded with Fluo-4 AM dye, cerebral organoids were stimulated with CPGs and changes of fluorescent intensity were analyzed with an inverted microscope equipped with a sCMOS camera.

## RESULTS

Three different CPGs with different periods are used (1,7s, 2,9s and 5s). Outputs of the CPG are triggered with the Calcium imaging camera recording. The stimulation applied to the isolated organoid is a 4V pulse of 800 $\mu$ s. Each spike of the CPG occurs one stimulation on the organoid. We can notice that the living organoid dynamically reproduced the pattern of oscillation applied by the CPG.



## CONCLUSIONS

This biomimetic CPGs are working in real-time and can send biomimetic stimulations on living organoid. We validate the stimulation using Calcium imaging response. This bio-hybrid system will be used for investigating network dynamics in organoid and for controlling living cells to activate in a specific temporal pattern [4].

## REFERENCES

- [1] M. Ambroise, et al., Real-time biomimetic Central Pattern Generators in an FPGA for hybrid experiments. *Frontiers in Neurosciences*, 7:215, November 2013
- [2] MA. Lancaster, et al., Cerebral organoids model human brain development and microcephaly, *Nature*, 501, 373-379, 2013
- [3] J. Kawada, S. Kaneda, T. Kirihara, A. Maroof, T. Levi, K. Eggan, T. Fujii, Y. Ikeuchi, Generation of a Motor Nerve Organoid with Human Stem Cell-Derived Neurons, *Stem Cell Report*, 9:5, 1441-1449, November 2017
- [4] AA. Hill, J. Lu, MA. Masino, OH Olsen, RL Calabrese, A model of a segmental oscillator in the leech heartbeat neuronal network, *J Comput Neuroscience*, 10, 281-302, 2001
- [5] M. Ambroise et al., Biomimetic neural network for modifying biological dynamics during hybrid experiments, *Journal on Artificial Life and Robotics*, 22:3, 398-403, September 2017

**KEYWORDS:** Neuromimetic, CPG, stimulation, organoid, bio-hybrid